Decision-making in otitis media in children, Part II: A cost-effectiveness analysis

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Acute otitis media (AOM) is a source of considerable expense of money and care. Two protocols for the empirical treatment of AOM are compared by a cost-effectiveness analysis. In protocol 1, treatment is initiated by a standard-spectrum antibiotic (amoxicillin) for 5–7 days; in case of clinical failure, a second treatment is prescribed with a wide-spectrum antibiotic (cefaclor) for 7–10 days. In protocol 2, treatment with a standard-spectrum antibiotic is prescribed only in case of clinical failure after a 'masterful inactivity' for 3–5 days, then checked on days 5–7, for a prescription of a wide-spectrum antibiotic in case of failure. The two protocols have a similar effectiveness, but the cost of protocol 2 is significantly higher because of a greater expense for medical visits. A low compliance rate is a definite factor of high cost-effectiveness ratio.

Key words: Otitis media, cost-effectiveness analysis, decision-making

INTRODUCTION

There are three important reasons to analyze the cost-effectiveness of diverse options to manage acute otitis media (AOM) therapy in current medical practice. First, this condition is very common. The reported annual incidence rate of AOM during the first 2 years of life is 1.14 episode per year [1]. Approximately 75% of the infants had at least one AOM episode, 50% had two and 25% had at least three episodes up to the age of 2 years [2,3]. Patients with AOM account for 12.4% of visits to office-based pediatricians and 1.7% to general practitioners. In addition, in about 20% of cases, a middle ear effusion persists for 6 weeks after treating acute otitis media, resulting in multiple visits and prolonged prescriptions [1,4].

Second, despite numerous investigations, precise diagnostic criteria for AOM remain uncertain [4]. With patients aged 0–12 months, the doctor depends primarily on examination of tympanic membranes or a history of otitis to make a diagnosis. Patients in this age group are the most difficult to examine because of the small diameter of their ear canals and the lack of cooperation. The child is usually crying and irritable, making otoscopic examination difficult. As the clinician struggles to reach a decision as to whether AOM is present, the crying by the child will almost certainly make the tympanic membrane appear somewhat red. The temptation is great to conclude that the child does indeed have an ear infection requiring antimicrobial treatment. There is often an unspoken agreement between the parent and the physician that a prescription for antibiotics justifies the office visit. Because amoxicillin as first-line therapy is considered to be extremely safe and benign, even when the diagnosis is questionable or uncertain, the pact can be fulfilled with minimal risk with satisfaction to both the parent and physician. The fact that doctors have been very certain of the diagnosis in only 58% of children aged 0–12 months is disconcerting because this age group has the highest incidence of otitis media [4]. Diagnosis reliability, however, is important because treatment is given even when imprecise criteria are used, when the risks of the condition, and the expected benefits of treatment, are not established [5].

Third, multiple treatment options for AOM have been proposed. Early investigators reported better outcomes and lesser rates of complications when AOM was treated with antibiotics than with a placebo, but recent studies haved failed to show significant clinical

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differences [6,7]. A famous Dutch study [5] which reported no difference in outcome among patients treated with antibiotics, myringotomy, antibiotics combined with myringotomy or placebo may have been partly responsible for the low or delayed use of antibiotics by Dutch practitioners. The proportion of patients prescribed antibiotics varies greatly among the countries, from 31.2% in The Netherlands to 98.2% in both Australia and New Zealand, as did the duration of treatment [4]. The optimal duration of administration of antibiotics is uncertain, with 2–3- and 5-day courses reported as being as effective as 7–10-day courses [8,9]. Prepacking of antibiotics into 5-day aliquots may account for the British doctors prescribing antibiotics for 5 days [10]. These discrepancies have considerable consequences for medical care: a 5-day course rather than a 10-day one would save more than $50 million in the USA, based on the most conservative estimate of prescribing rates [4].

Many experts recommend amoxicillin for the initial empirical treatment of all episodes, although some of them limit this to situations where β-lactamase-producing organisms are unexpected in the light of epidemiologic considerations. Others suggest initial treatment with a β-lactamase-stable drug because of an increased prevalence of amoxicillin-resistant organisms. Another approach, popular in The Netherlands, is to restrict antimicrobial therapy to children continuing to have symptoms after 24–72 h of 'masterful inactivity' because of a high rate of spontaneous resolution of acute symptoms [7].

A MEDICO-ECONOMIC ANALYSIS

Treatment protocols

The objective is to answer the question of how two management options for the initial treatment of AOM in children differ with respect to their medico-economic efficiency in terms of their cost-effectiveness ratios:

Protocol 1—Initial prescription of a standard-spectrum drug sensitive to β-lactamase (treatment A) for all patients with AOM: oral amoxicillin 50-75 mg per kg of body weight daily or 250 mg thrice daily, for 7 days with an average clinical success rate of 0.90. A second visit V2 is scheduled on the fifth or seventh days to check the state of the disease, cure or presence of middle ear effusion (MEE). If MEE is observed, a new treatment (treatment B) is prescribed with a wide-spectrum antibiotic, usually cefaclor for 7–10 days. Patients are re-examined on completion of treatment B and 30 days later to determine whether they have been successfully cured.

Protocol 2—Initial symptomatic therapy with decongestant nose drops and analgesics, with no prescription of antibiotics. The second visit V2 is scheduled 3–5 days later to check the disease state, cure or presence of MEE/complication. If systemic or local signs persist—for approximately 15% of children more than 2 years of age—antibiotic treatment with a standard-spectrum antibiotic (treatment A) is prescribed for 5–7 days, then checked on the seventh to tenth days in the same way as in protocol 1.

Estimation of costs

Costs may be evaluated from several perspectives—e.g. the patient's family, the institution, the insurance system or society [1]. Despite the fact that the optimal perspective is the societal one which encompasses the true opportunity costs of all resources used, the present analysis will consider direct charges, payments or expenditure paid to providers, including physicians, pharmacies and hospitals: for physician visits and care, tympanocentesis and myringotomy, audiology tests, surgery for ventilating tubes (grommets), microbiological procedures and antibiotics. Costs will not take into account indirect costs, parental lost wages and travel expenses, or the cost of the time that parents spend obtaining care for their child. If the initial approach fails to cure otitis media, the risk of prolonged MEE and/or complications will be increased, and the family will be burdened with medical costs for a second medication, additional office visit fees and time lost from employment.

This analysis is limited to the direct charges of the acute phase of the disease. Antibiotic costs are quantified at standard daily acute otitis media dosages, i.e. amoxicillin 50 mg/kg and cefaclor 40 mg/kg. Dosage is adjusted to a patient weight of 12 kg related to a child 2 years old.

The effectiveness of each protocol is the difference between its expected result or outcome and the outcome of untreated AOM. Cost and outcome are estimated in the 'real world', e.g. in the actual conditions of practice with reduced compliance, eventually concurrent diseases or treatments and competing risk factors. The cost of untreated AOM is assumed to be nil.

Decision tree and cost-effectiveness ratio

The decision tree is constructed from left to right (Figure 1). The square nodes represent 'choice' or prescription decisions, and the circular nodes represent 'chance' events. The patient is defined as 'compliant'

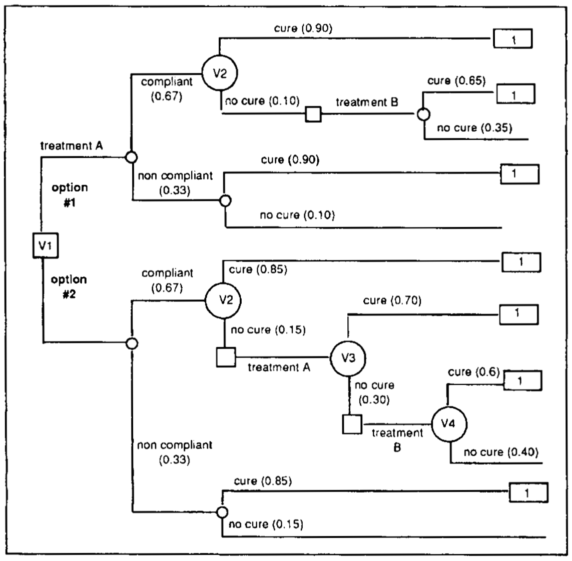

Figure 1 Decision tree for comparing the effectiveness of two protocols for the treatment of the acute phase of AOM. V1 and V2 are the scheduled medical visits and periodic otoscopic examinations. Respective probabilities are in parentheses ( ).

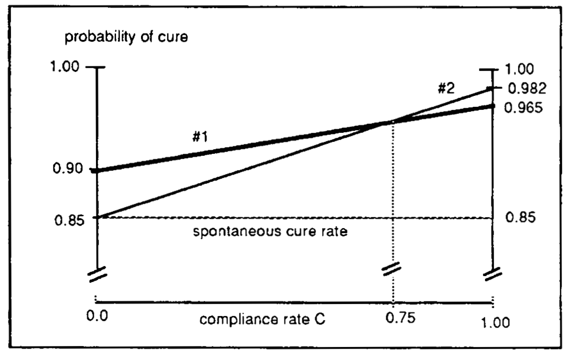

Figure 2 Expected cure rate of the two protocols according to the compliance rate C.

when he or she undergoes the regular follow-up visits and completes the prescribed treatments. The compliance rate is the proportion of patients who comply with the medical appointments and prescriptions. About two thirds of patients (0.67) turn out to be compliant with the treatment prescribed and scheduled visits [8].

Folding back the decision tree from right to left gives the average expected cure rate of each protocol:

protocol 1:

$$(1\times0.90+1\times0.65\times0.10)\times0.67+1\times0.90\times0.33=0.944$$

protocol 2

$$\{1\times0.85+[1\times0.70+(1\times0.60\times0.30)]\times0.15\}\times0.67+1\times0.85\times0.33=0.938$$

Cure rates of the two protocols are very close. It emerges that the main component of clinical success is the compliance rate—e.g. the proportion of patients who comply with the follow-up visits and periodic otoscopic re-examinations.

The cure rate according to the compliance rate C will be:

protocol 1

$$(1\times0.90+1\times0.65\times0.10)\times C+1\times0.90\times(1-C)=0.90+0.065\times C$$

protocol 2:

$$\{1\times0.85+[1\times0.70+(1\times0.60\times0.30)]\times0.15\}\times C+1\times0.85\times(1-C)=0.85+0.132\times C$$

The probability of cure is a linear function of the compliance rate C, illustrated by Figure 2.

The two protocols give the same expected cure rate when the compliance rate C is 0.75, e.g. when three out of four patients comply with the medical prescriptions and otoscopic periodic examinations. When the compliance rate is higher than 0.75, protocol 2 gives a better cure rate than protocol 1; the reverse is true if less than three out of four children comply with medical prescriptions.

Effectiveness is estimated by the difference of the clinical success rate of each protocol and the baseline or spontaneous cure rate 0.85.

Protocol 1 effectiveness is: $0.944-0.85=0.094$;
or according to the compliance rate C:
$(0.90+0.065\times C)-0.85=(0.05+0.065\times C)$

Protocol 2 effectiveness is: $0.938-0.85=0.088$;
or according to the compliance rate C:
$(0.85+0.132\times C)-0.85=0.132\times C$

The *marginal effectiveness,* or difference between the effectiveness of protocol 1 and that of protocol 2, is $(0.05+0.065\times C)-0.132\times C=0.05-0.067\times C$. Outcome in favor of protocol 1 is reliable only when the compliance rate is very low.

The effectiveness of the two protocols is quite similar, at least when the compliance rate value lies within a reasonable range. Therefore, the cost-effectiveness ratios of the two protocols are mostly dependent on their respective costs, as they may be read on the decision tree (Figure 1).

The cost of protocol 1 firstly includes the cost of the visit V1, and the cost of treatment A with amoxicillin for 5–7 days. The follow-up expenses, cost of V2 and cost of treatment B depend on the compliance rate C:

The cost of protocol 1 is $V1+A+C\times(V2+0.10\times B)$

The cost of protocol 2 includes:
$V1+C\times[V2+0.15\times(A+V3)+0.30\times(B+V4)]$.

The *marginal cost* is the difference between the costs of protocols 1 and 2:

$$\begin{aligned}&(\text{Cost of protocol 1})-(\text{cost of protocol 2})\\&=[V1+A+C\times(V2+0.10\times B)]-[V1+C\times\\&\quad(V2+0.15\times(A+V3)+0.30\times(B+V4)]\\&=A-C\times(0.15\times A+0.2\times B+0.15\times V3+0.3\ V4).\end{aligned}$$

The *marginal cost-effectiveness ratio* between protocols 1 and 2 is a hyperbolic function of the compliance rate C:

$$\frac{A-C\times(0.15\times A+0.2\times B+0.15\times V3+0.3\times V4)}{0.05-0.067\times C.}$$

Application

Applied to a child weighing 12 kg, treatment A with amoxicillin 50 mg/kg for 5 days uses 3000 mg with a cost of 22 ff. Treatment B with cefaclor 20 mg/kg for seven days will use two packages with a total cost of approximately 80 ff; the assumed average cost of a medical visit is 150 ff. The cost-effectiveness ratios of the two protocols, depending on two compliance rates C, should be:

	Compliance rate 0.67	Compliance rate 1.00
protocol 1	278/0.094=2957 ff	330/0.115=2870 ff
protocol 2	314/0.088=3568 ff	395/0.132=2992 ff

The cost-effectiveness ratio expresses the cost of one clinical cure that is attributable to the medical prescription. Medical visits are much more expensive than medical prescriptions. Therefore, in spite of saving more medical prescriptions, protocol 2 turns out to be more expensive than the systematic antibiotic prescription for all AOM episodes according to protocol 1.

Nonetheless, the real question lies in the respective costs of the clinical failure rates of the two protocols, or *future costs* of the treatment protocols of the acute phase of AOM. Failure rate=(1–cure rate) is linearly related to compliance rate C. The difference between the respective failure rates of the protocols 1–2

$$=[1-(0.05+0.065\times C)]-(1-0.132\times C)=0.067\times C-0.05$$

The difference between failure rates is negative, in favor of protocol 2, as soon as the compliance rate C is higher than 0.75.

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